GPR64 NUCLEOTIDE SEQUENCE (SEQ ID NO: 1)

Gene name: G protein-coupled receptor 64

Unigene number: Hs.421137
Probeset Accession #: AA435577
Nucleic Acid Accession #: NM_005756.1

Coding sequence: 73-3117 (underlined sequences correspond to start and stop

codons)

1	11	21	31	41	51	
1	1		1	1	Ī	
AGCCAGCCCG	AGGACGCGAG	CGGCAGGTGT	GCACAGAGGT	TCTCCACTTT	GTTTTCTGAA	60
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	CGTTCAAGAT					180
	AAGATACTGA					240
	CCCCCTCCTC					300
	CTTCAAACGA					360
	TCAAACCCCA					420
	GAGGTGAGAT				TCCCCAGAAT	480
	CGAATGGCAC					540
	AAACCCTGCA					600
	GCACATTAAA					660
	TAGCCGCTTT TACCCTGCCC					720
	TTGTCTGTCT			GAAAGCTTCA		780
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	CAGATTATTC					900 960
			ATAGCTTCCA		TGACATGCCC	1020
				ATGTCTCCGG		1020
	CCTCATTTTC					1140
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	AGATGGAGAA					1260
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	TGCTGAAAGT				TTCAAACACG	1380
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				CATCGCTGAT		1560
	ACATGGAGCT					1620
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GTTGCAAACC	TGACCGTCAG	GAACTTGACA	AGAAACGTGA	CAGTCACATT	AAAGCACATC	1740
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	GCTGGTCAGA					1860
	GTAGCCATCT CTCAAATGAT				TAGGACATCT	1920
	TGTCAGTGAC				TGGGCTTTCA	1980
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CTCCTGGACT				TCTGCTGAA		2100
	ATTTTCTCTT	GGTCTCATTC	ACATGGATGG	CCTAGAAGC	AGIGGCIGIA	2160 2220
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	GGGGGTACC					2340
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CTGAACGTCA	GCATGTTCAT	TGTGGTCCTG	GTTCAGCTCT	GTCGAATTAA	AAAGAAGAAG	2520
CAACTGGGAG	CCCAGCGAAA	AACCAGTATT	CAAGACCTCA	GGAGTATCGC	TGGCCTTACA	2580
	GAATAACTTG				TAACGTGACC	2640
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TGTGTGGCCA AAGAAAATGT CAGGAAGCAA TGGAGGCGGT ATCTTTGTTG TGGAAAGTTA 2760
CGGCTGGCTG AAAATTCTGA CTGGAGTAAA ACTGCTACTA ATGGTTTAAA GAAGCAGACT
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GTAAACCAAG GAGTGTCCAG CTCTTCAAAT TCCTTACAGT CAAGCAGTAA CTCCACTAAC
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TCCACCACAC TGCTAGTGAA TAATGATTGC TCAGTACACG CAAGCGGGAA TGGAAATGCT
                                                                   2940
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                                                                   3120
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                                                                   3180
CACAATGTGA GATGTATGAA AATCAACTCA TTTTATTCTC GGCAACATCT GGAGAAGCAT
AAGCTAATTA AGGGCGATGA TTATTATTAC AAGAAGAAAC CAAGACATTA CACCATGGTT 3300
TTTAGACATT TCTGATTTGG TTTCTTATCT TTCATTTTAT AAGAAGGTTG GTTTTAAACA 3360
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                                                                   3480
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                                                                   3720
TCAAGAAATA ATGATCCCAG CCAGACTGAG AAAATGTAAG CAGACAGTGC CACAGTTAGC
                                                                   3780
TCATACAGTG CCTTTGAGCA AGTTAGGAAA AGATGCCCCC ACTGGGCAGA CACAGCCCTA
                                                                   3840
TGGGTCATGG TTTGACAAAC AGAGTGAGAG ACCATATTTT AGCCCCACTC ACCCTCTTGG
                                                                   3900
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CCCCAGTAGT CAGATTATAG AATCTGCACC AAGATGTTTA GCTTTATACC TTGGCCACAG
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TATACAGGGT CTATCTTGCT TCCTACCTAC ATCTGCTTGA GCAGTGCCTC AAGTACATCC
TTATTAGGAA CATTTCAAAC CCCTTTTAGT TAAGTCTTTC ACTAAGGTTC TCTTGCATAT
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                                                                   4560
CTGACTTGTC TTTGCAATAT TTCTTTTCTG ATTTATTTAA TTTTCTTGTA TTTATATGTT
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AAAATCAAAA ATGTTAAAAT CAATGAAATA AATTTGCAGT TAAGA
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GPR64 AMINO ACID SEQUENCE (SEQ ID NO:2)
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Gene name: G protein-coupled receptor 64

Unigene number: Hs.421137
Protein Accession #: NP_005747.1
Signal sequence: 1-38

GPS domain: 564-615

Transmembrane domains: 624-646, 660-682, 688-710, 733-755, 783-805.

828-850, 858-880

Cellular Localization: plasma membrane

1	11	21	31	41	51	
1	1	1	1	Ī	Ī	
MVFSVRQCGH	VGRTEEVLLT	FKIFLVIICL	HVVLVTSLEE	DTDNSSLSPP	PAKLSVVSFA	60
PSSNEVETTS	LNDVTLSLLP	SNETEKTKIT	IVKTFNASGV	KPQRNICNLS	SICNDSAFFR	120
			SELKRSELNK			180
			MEHCCCSVRI			240
			PKATSFAEPP			300
PQPSAPIASS	PAIDMPPQSE	TISSPMPQTH	VSGTPPPVKA	SFSSPTVSAP	ANVNTTSAPP	360
VQTDIVNTSS	ISDLENQVLQ	MEKALSLGSL	EPNLAGEMIN	QVSRLLHSPP	DMLAPLAORL	420
			RVNASSFNTT			480
NSIGTITLPS	SLMNNLPAHD	MELASRVQFN	FFETPALFQD	PSLENLSLIS	YVISSSVANL	540

TVRNLTRNVT	VTLKHINPSQ	DELTVRCVFW	DLGRNGGRGG	WSDNGCSVKD	RRLNETICTC	600
SHLTSFGVLL	DLSRTSVLPA	QMMALTFITY	IGCGLSSIFL	SVTLVTYIAF	EKIRRDYPSK	660
ILIQLCAALL	LLNLVFLLDS	WIALYKMQGL	CISVAVFLHY	FLLVSFTWMG	LEAFHMYLAL	720
	YILKFCIVGW					780
AVFYITVVGY	FCVIFLLNVS	MFIVVLVQLC	RIKKKKQLGA	QRKTSIQDLR	SIAGLTFLLG	840
	GPVNVTFMYL					900
NSDWSKTATN	GLKKQTVNQG	VSSSSNSLQS	SSNSTNSTTL	LVNNDCSVHA	SGNGNASTER	960
NGVSFSVQNG	DVCLHDFTGK	QHMFNEKEDS	CNGKGRMALR	RTSKRGSLHF	IEOM	

NUCLEOTIDE AND AMINO ACID SEQUENCES OF GPR64 ANTIBODY CLONES (CDR regions are shown bolded and underlined.)

NUCLEOTIDE SEQUENCES

SEQ ID NO:3: GPR64-1 Heavy Chain Variable Region:

GATGTGCAGCTTCAGGAGTCGGGACCTGGCCTGGTGAAACCTTCTCAGTCTCTG
TCCCTCACCTGCACTGTCACTGGCTACTCAATCACCAGTGATTATGCCTGGAA
CTGGATCCGGCAGTTTCCAGGAAACAAACTGGAGTGGCTGGGCTACATAAGCT
TCAATGATAACACTAACTACAACCCATCTCTCAAAAGTCGAATCTCTATCAC
TCGAGACACACCCATCTCTCCAGGTTGAATTCTGTGACTACTGA
GGACACAGCCACATATTACTGTACAAGGAGGGTGGACTACTGGGGTCAAGGA
ACCTCAGTCACCGTCTCCTCA

SEQ ID NO:4: GPR64-1 Light Chain Variable Region

SEQ ID NO:5: GPR64-16 Heavy Chain Variable Region

CAGGTTACTCTGAAAGAGTCTGGCCCTGGGATATTGCAGCCCTCCCAGACCCTC
AGTCTGACTTGTTCTTCTCTGGGTTTTCACTGAGCACTTCTGGTGTGGGTGT
GAGCTGGATTCGTCAGCCTTCAGGAAAGGGTCTGGAGTGGCACACATTT
ACTGGGATGATGATAAGCGCTATAACCCATCCCTGAAGAGCCGGCTCACAA
TCTCCAAGGATACCTCCAGAAACCAGGTATTCCTCAAGATCACCAGTGTGGACA
CTGCAGATACTGCCACATACTGTGCTCGAAGAGTATTCATTATTACGGCC
TTTGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA

SEQ ID NO:6: GPR64-16 Light Chain Variable Region

SEQ ID NO:7: GPR64-18 HEAVY CHAIN VARIABLE REGION

SEQ ID NO:8: GPR64-18 Light Chain Variable Region

AGTATTGTGATGACCCAGACTCCCAAATTCCTGCTTGTCTCAGCAGGAGACAGG
ATTACCATAGCCTGCAGGGCCAGTCAGAGTGTGAGTAATGATGTAGCT
ACCAACAGAAGCCAGGGCAGTCTCCTAAACTGCTGATAAACTATACATCCAAT
CGCTACACTGGAGTCCCTGATCGCTTCACTGGCAGTGGATATGGGACGGATTT
CACTTCACCATCAGCACTGTGCAGGCTGAAGACCTGGCAGTTTATTTCTGTCA
GCAGGCTTATAGCTCTCCGTGGACGTTCGGTGGAGGCACCAAGCTGGAAATC
AAACGG

SEQ ID NO:9: GPR64-20 Heavy Chain Variable Region

GATGTGCAGCTTCAGGAGTCGGGACCTGGCCTGGTGAAACCTTCTCAGTCTCTG
TCCCTCACCTGCACTGTCACTGGCTACTCAATCACCAGTGATTATGCCTGGAA
CTGGATCCGGCAGTTTCCAGGAAACAAACTGGAGTGGATGGGCTACATAAGCT
ACAGTGATTACACTAGCTACAACCCATCTCTCAAAAGTCGAATCTCTATCAC
TCGAGACACACCCACTCTCTCAAAAGTCGAATTCTGTGACTACTGA
GGACACAGCCACATATTACTGTGCAAGAAGGGTGGACTACTGGGGTCAAGGA
ACCTCAGTCACCGTCTCCTCA

SEQ ID NO:10: GPR64-20 Light Chain Variable Region

SEQ ID NO:11: GPR64-48 Heavy Chain Variable Region

GATGTGCAGCTTCAGGAGTCGGGACCTGGCCTGGTGAAACCTTCTCAGTCTCTG
TCCCTCACCTGCACTGTCACTGGCTACTCAATCACCAGTGATTATGCCTGGAA
CTGGATCCGGCAGTTTCCAGGAAACAAACTGGAGTGGATGGGCTACATAAGCT
TCAGTGATAGCACTACCAACCCATCTCTCAAAAGTCGAATCTCTATCAC
TCGAGACACACCCATCTCTCCAGGTTGAATTCTGTGACTACTGA
GGACACAGCCACATATTACTGTGCAAGAAGGGGGGGACTACTGGGGTCAAGGA
ACCTCAGTCACCGTCTCCTCA

AMINO ACID SEQUENCES

SEQ ID NO:13: GPR64-1 Heavy Chain Variable Region
DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKLEWLGYISFND
NTNYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTATYYCTRRVDYWGQGTSVTVS
S

SEQ ID NO:14: GPR64-1 Light Chain Variable Region
DVVMTQTPLSLPVSLGDQASISCRSSQSLVHSNGNNYLHWYLQKPGQSPKLLIYK
VSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPWTFGGGTKLEIK

SEQ ID NO:15: GPR64-16 Heavy Chain Variable Region
QVTLKESGPGILQPSQTLSLTCSFSGFSLSTSGVGVSWIRQPSGKGLEWLAHIYWD
DDKRYNPSLKSRLTISKDTSRNQVFLKITSVDTADTATYYCARRVFIITAFDYWGQ
GTTLTVSS

SEQ ID NO:16: GPR64-16 Light Chain Variable RegionDIQMTQTTSSLSASLGDRVTISC**RASQDISNYLN**WYQQKPDGTVKLLIY**YTSNLHS**GVPSRFSGSGSGADYSLTIGNLEQEDIATYFC**QQGNTLPWT**FGGGTKLEIK

SEQ ID NO:17: GPR64-18 Heavy Chain Variable Region
QVSLKESGPGILQPSQTLSLTCSFSGFSLSTSGMGVSWIRQPSGKGLEWLAHIYWDDKRYNPSLKSRLTISKDTSSNLVFLKITSVDTADTATYYCARREVRRDYYAMDYWGQGTSVTVSS

SEQ ID NO:18: GPR64-18 Light Chain Variable Region
SIVMTQTPKFLLVSAGDRITIAC<u>RASQSVSNDVA</u>WYQQKPGQSPKLLIN<u>YTSNRYT</u>
GVPDRFTGSGYGTDFTFTISTVQAEDLAVYFC<u>QQAYSSPW</u>TFGGGTKLEIK

SEQ ID NO:19: GPR64-20 Heavy Chain Variable Region
DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKLEWMGYISYS
DYTSYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTATYYCARRVDYWGQGTSVTV
SS

SEQ ID NO:20 GPR64-20 Light Chain Variable Region
DVVMTQTPLSLPVSLGDQASISCRSSQSLVHSNGNTYLHWYLQKPGQSPKLLIYK
VSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPWTFGGGTTLEIK

SEQ ID NO:21: GPR64-48 Heavy Chain Variable Region
DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKLEWMGYISFSDSTSYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTATYYCARRGDYWGQGTSVTVSS

SEQ ID NO:22: GPR64-48 Light Chain Variable Region

DVVMTQTPLSLPVSLGDQASISC**RSSQSLVHSNGNTYLH**WYLQKPGQSPKLLIY**K VSNRFS**GVPDRFSGSGSGTDFTLKISRVEAEDLGVYFC**SQSTHLPW**TFGGGTKLEIK

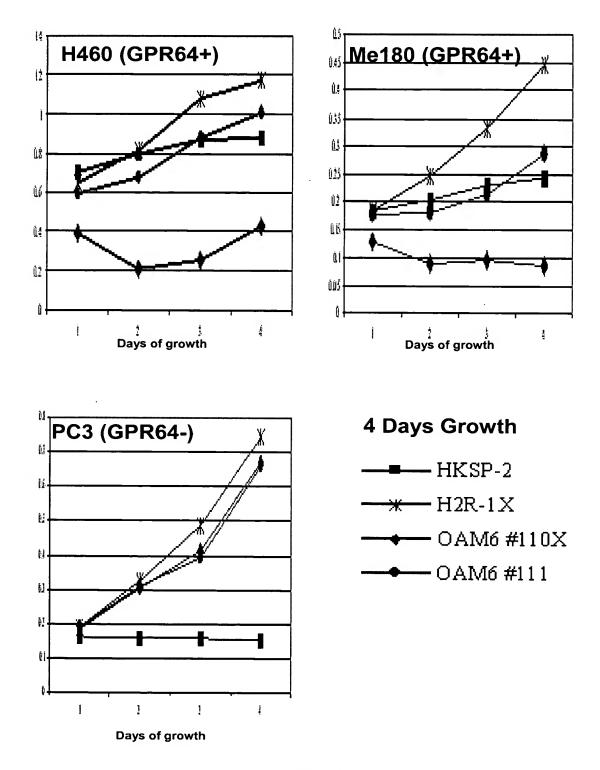


FIG. 3

GPR+ Cells

	FACS	MTT
RNA+	expression	<u>effect</u>
ME180	+	+
H460	+	+ .
H520	+	+
C32	+	-
DU145	+	-

GPR64- Cells

	FACS	MTT		FACS	MTT
RNA+	expression	effect	RNA-	expression	effect
BT474	-		HT1376	ND	-
MCF7	-	_	SW780	-	+
NW231	-	_	HCT116	ND	_
H358	_	-	SW620	ND	_
Calu6	-	_	U87	-	_
SKOV3	-	_	A549	_	-
LnCAP	_	+	A375	-	-
2110711		•	C8161	-	-
				-	-
			ES2	-	-
			OV-90	ND	-
			OVCAR3	-	-
			PA-1	ND	-
			PC3	-	-

Fig. 4

Mab	FACS (nM)	HC	Ŧ	Biacore	Isotype	Mab	FACS (nM)	HC	4	Biacore	Isotype
61a	0.7288	3+	2+	1.09E-09	2b	85a	38.2	2+	2+	2.78E-09	
62a	2.736	2+	2+	1.73E-09	2b	86a	97.98	ned	+		
65a	1.371	2+	2+	1.48E-09	2b	87a	77.04	nea	ŀ		
68a	6.15	2+	+		-	88a	37.51	nea			
70a	1.831	3+	2+	1.22E-09	2b	89a	107	ned led			
80a	0.4032	2+	+		_	90a	194.6	2+	2+		
67a	246.1	2+				91a	4.252	3+	2+		
69a	295.6	neg				93a	1.269	2+	+	8.01E-09	
71a	8.159	2+	1	And the second s		94a	87.84	2+	2+	1.66E-07	
72a	130.8	neg	ı			95a	28.81	3+	2+	6.29E-10	2b
74a	442.6	5+	ı			96a	22.77	2+			
75a	102.4	2+	2+	9.68E-09		97a		ā			
76a	0.8313	2+	2+	1.62E-10	2a	98a	186.1	5			
77a	0.9765	3+	+	2.07E-09	-	99a	10.96	2+	2+	6.97E-09	_
78a	8.955	2+	+	4.06E-11	2a	100a	42.1	2+	2+	1.81E-09	
79a	5.299	3+	1+			101a	4.939	3+	2+	1.46E-10	
81a	0.0585	2+	++	1.38E-08	-	102a	117.2	ы			_
82a	5.829	2+	2+	1.61E-09		103a		Б	١.		2a
83a	124.7	2+				46Z		3+			
84a	113.6	2+	ı		2a	77b		2			
18b1	~4.0	2+	+	2.83E-09	-	104		pd	T		

Fig. 5

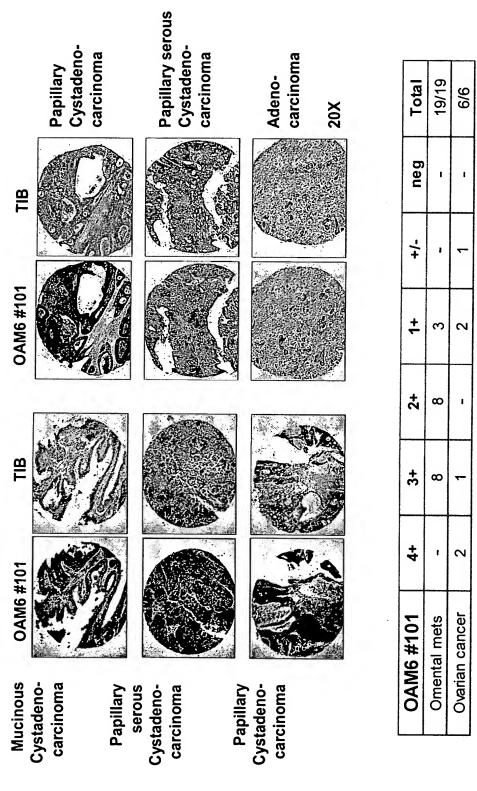


FIG. 6

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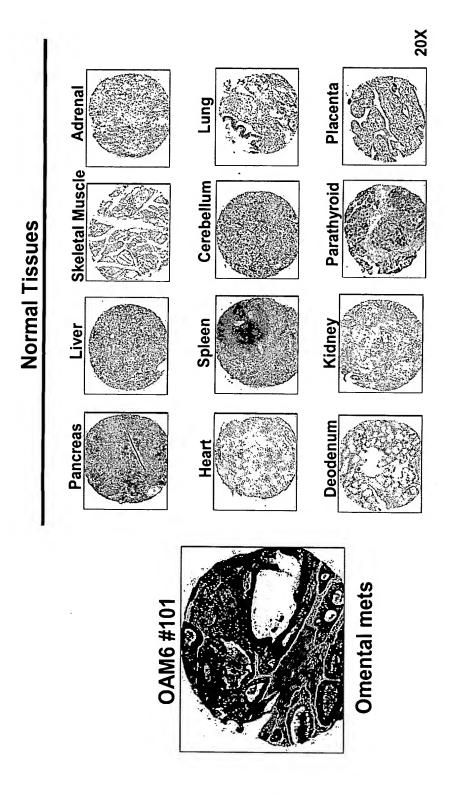


FIG. 7

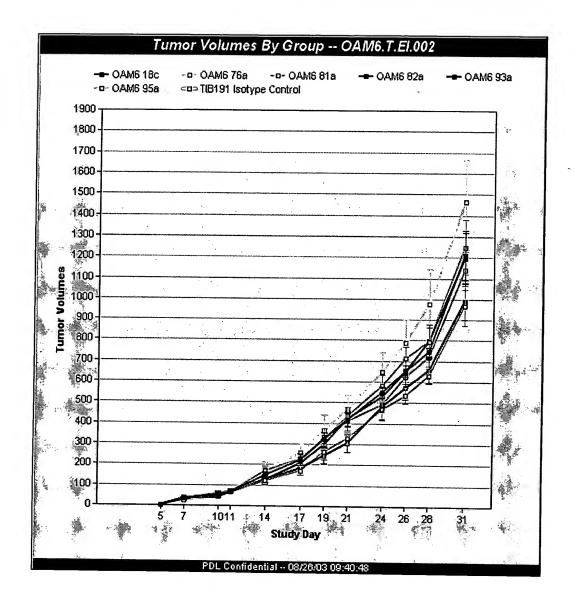


FIG. 8

MTT assay: H460 survival after 4d treatment with ADCs

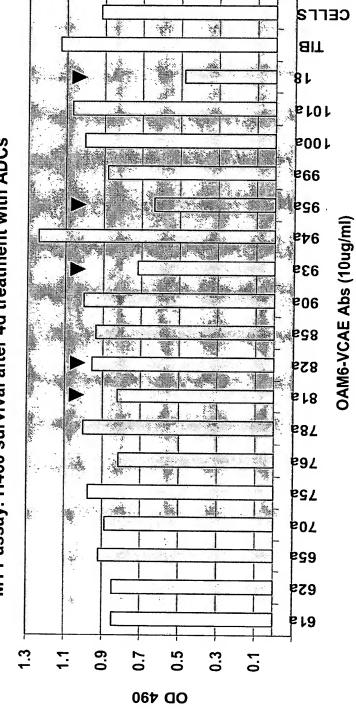


FIG. 9

FIG. 10